UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Carmen Rodia, Risk Manager

From: Virna Stillwaugh, PhD, Entomologist

Secondary Review: Jennifer Saunders, PhD, Senior Biologist

Date: 3/18/2019

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

THIS DER DOES NOT CONTAIN CONFIDENTIAL BUSINESS INFORMATION

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcodes: 449549
Decision no.: 542707
Submission no:1022186
Action code: R350.1
Product Name: RMI-2011-D 0.04% Diflubenzuron Cattle Supplement
EPA Reg. No or File Symbol: 89459-3
Formulation Type: Granular
Ingredients statement from the label with PC codes included:
RMI-2011-D: Diflubenzuron 0.04% PC code: 108201

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate):
Granular insect growth regulator nutritional supplement (Diflubenzuron 0.04%). For use in sheep, goat and deer is 0.40 mg Diflubenzuron/kg of body weight. The following table can be used to determine the exact amount of this product needed based on the weight of each animal to be treated:

Species	Body weight	Oz of RMI-2011-D 0.04% Diflubenzuron Cattle Supplement
Sheep, goats and deer	Up to 50 lbs (22.7 Kg)	0.8
	51-100 lbs (23.1-45.4 Kg)	1.6
	101-150 lbs (45.8-68 Kg)	2.4
	151-200 lbs (68.5-90.7 Kg)	3.2
	201-250 lbs (91.2-113.4 Kg)	4.0

For larger sheep, goats and deer, over 250 lbs of body weight, feed and additional 0.8 ounces, for each additional 50 lbs of body weight.

Use Patterns:
Oral granular insect growth regulator nutritional supplement that prevents the emergence of adult horn flies, face flies, house flies and stable flies from manure waste of treated cattle, horses, swine, sheep, goats and deer through the fly season. Can be used as part of an integrated/complete fly pest management program. Existing adult flies will

not be affected. Start feeding before flies appear and continue to use until cold weather marks the end of fly season.

I. Action Requested: Efficacy review of 2 MRIDs (50624202 and 50624203) in support of efficacy of Diflubenzuron feedthrough insecticides against house and stable flies in sheep, deer and goat for 89459-3 (RMI-2011-D 0.04% Diflubenzuron Cattle Supplement).

II. Background:
The registrant has submitted efficacy data (MRIDS 50624202 and 50624203) of Diflubenzuron products in stable flies and houseflies in goats in support of a PRIA R350.1 label amendment to add directions for use for feeding sheep, goats and deer. Similar uses for feeding cattle, horses and swine were previously approved for this product.

III. MRID Summary:

MRID 50624202. Smythe, B. (2017*)* Efficacy of Diflubenzuron Against Stable Flies Developing in Manure from Treated Animals 4: Final Report. Project Number: 5137. Unpublished study prepared by New Mexico State University. 24p.

(1) **GLP or non-GLP**
Non-GLP

(2) **Methods:**
This was a live animal/lab study conducted at the NMSU Veterinary Entomology research lab. The test substance was ClariFly Larvicide Livestock Premix 0.67% (=RMI-2011-C 0.67% Diflubenzuron Cattle Supplement), a dry mix of feed ingredients and active ingredients. The study was conducted using 24 domesticated male goats with a weight range of 40-100 lbs, divided into 4 groups (3 treatments and one control). Treated goats were dosed with the amounts of diflubenzuron, mixed with their daily feed for 9 d, indicated below:

- Group 1: 0.15 mg of diflubenzuron/kg of body weight/day
- Group 2: 0.20 mg of diflubenzuron/kg of body weight/day
- Group 3: 0.30 mg of diflubenzuron/kg of body weight/day
- Group 4: control (untreated: fed in the same manner minus the active ingredient)

All animals received the same dose of product based on their weight, beginning on study day 0 through study day 9. All animals consumed fully the treatment in their first half of their diet (morning feeding). The remainder of the diet was administered in the afternoon. Clean water was provided *ad libitum*. Manure samples (~200 g) from each animal was collected in bags, beginning in day 0 (pretreatment) through day 9. For each goat on each collection day, three stable fly bioassay cups were prepared using the feces on a given collection day. Manure samples were frozen to kill any arthropod fauna that may have been present in the feces prior collection and then thawed prior to use. Water was added to feces at rate of approximately 100 ml/50 g of feces and was mixed thoroughly by hand to ensure a homogeneous sample mixture. Approximately 50 g of amended manure mixture was placed in each plastic bioassay cup. Stable fly (*Stomoxys calcitrans*) larvae (<24 hours old) were collected, and 50 larvae were placed in each cup containing a feces sample. Bioassay cups were then placed into a #4 paper bag, with the top folded in triplicate and stapled to prevent adult stable fly escape. The paper bags were held at 80 °F, 12:12 LD, and approximately 40% RH, for a period of 3 weeks. Each bioassay cup was moistened with approximately 5 ml of water every 72 hours, until pupae were observed, to minimize desiccation of larvae.

Fly emergence was determined by counting the number of dead adult flies in each bioassay container, approximately 3 weeks after infestation. The percent efficacy of the three treatment groups was calculated with the following equation:

$$\%\ \text{Efficacy} = \left(\frac{\text{Control AAFE} - \text{Treatment AAFE}}{\text{Control AAFE}}\right) \text{x} 100$$

"AAFE" stands for "average adult fly emergence," the averages being of individual emergence data for each of the six animals (18 cups) within the specific group per day in question.

(3) **Results:**

Group 1 (0.15 mg diflubenzuron/kg of body weight/day)
Average percent adult fly emergency was 54.44%, 39.44%, 19.56%, 4.12%, 0.34%, 2.66%, 1.88%, 2.12%, 1.78%, and 1.34% on days 0, 1, 2, 3, 4, 5, 6, 7, 8, and 9, respectively. Percent efficacy was 8.03%, 66.98%, 93.19%, 99.40%, 95.49%, 96.85%, 96.60%, 97.31% and 97.69% on days 1, 2, 3, 4, 5, 6, 7, 8, 9, respectively.

Group 2 (0.20 mg diflubenzuron/kg of body weight/day)
Average percent adult fly emergence was 27.12%, 39.44%, 0.22%, 0%, 0.12%, 2.56%, 1.88%, 2.78%, 2.22% and 1.34% on days 0, 1, 2, 3, 4, 5, 6, 7, 8, and 9, respectively. Percent efficacy was 8.09%, 99.62%, 100%, 99.80%, 95.68%, 96.85%, 95.53%, 96.64% and 97.69% on days 1, 2, 3, 4, 5, 6, 7, 8 and 9, respectively.

Group 3 (0.30 mg diflubenzuron/ kg of body weight/day)
Average percent fly emergence was 35.88%, 34.66%, 0.44%, 0.34%, 2.00%, 3.34%, 0.56%, 5%, 1.44% and 1.12% on days 0, 1, 2, 3, 4, 5, 6, 7, 8 and 9, respectively. Percent efficacy was 19.17%, 99.25%, 99.45%, 99.41%, 94.36%, 99.07%, 91.95%, 97.82% and 98.08% on days 1, 2, 3, 4, 5, 6, 7, 8 and 9, respectively.

Group 4 (untreated control)
Control fly emergency was on average 39.34%, 42.88%, 59.22%, 60.34%, 55.66%, 59.12%, 59.88%, 62.12%, 66.12% and 57.78% on days 0, 1, 2, 3, 4, 5, 6, 7, 8, and 9, respectively.

Overall, >90% reduction in adult stable flies (*Stomxys calcitrans*) emergence numbers was observed by day 2 of the treatment compared to controls, except for the lower rate tested (0.15 mg diflubenzuron/kg of body weight/day), where 90% reduction of adult flies occurred on day 3. From day 2 and beyond, average emergence rates for the controls exceeded >50% of the original inoculum and data showed that emergency in the treatments was at least one order of magnitude lower in the controls, except for the lower rate (0.15mg of diflubenzuron/kg of body weight /day) whose emergency at day 2 wasn't an order of magnitude lower than the control.

(4) **Conclusion:** This MRID is **acceptable;** the data submitted supports efficacy of daily doses of the labeled rate (0.4 mg diflubenzuron/kg of body weight) to control stable flies on goat and sheep, but not deer, manure. The data indicated that daily doses of RMI-2011-C Granules at 0.15 mg of diflubenzuron/kg of body weight/day to goats reduced numbers of adult stable flies that emerged from manure during treatment by ≥90% compared to controls. The tested dose for active ingredient diflubenzuron using RMI-2011-C was less than the recommended label rate for RMI-2011-D 0.04% Diflubenzuron Cattle Supplement; these data can be bridged to support the label rate for RMI-2011-D 0.04% Diflubenzuron Cattle Supplement. Data can be bridged between Bovid species (goat and sheep) because they occupy similar habitats and graze on similar foods. Data cannot be bridged from goats to deer (Cervids) because they live in different habitats and require higher quality and less abrasive food than Bovids due to differences in their teeth (Heywood, 2009). Feeding habits difference (different food) between Cervids and bovids may affect feces fermentation needed for stable fly development.

MRID 50624203. Smythe, B.; White, C. (2018*)* Efficacy of Diflubenzuron Against House Flies Developing in Manure from Treated Animals 4: Final Report. Project Number: 5464. Unpublished study prepared by New Mexico State University. 25p.

(1) GLP or non-GLP
Non-GLP

(2) **Methods:**
This was a live animal/lab study conducted at the NMSU Veterinary Entomology research lab. The test substance was RF2279 015 DFB BAL (0.015% diflubenzuron), a pelleted feed. The study was conducted using 24 domesticated male goats with a weight range of 40-100 lbs, divided into 4 groups (3 treatments and one control). Treated goats were dosed with the amounts of diflubenzuron, mixed with their daily feed for 9 d, indicated below:

- Group 1: 0.40 mg of diflubenzuron/kg of body weight/day
- Group 2: 0.50 mg of diflubenzuron/kg of body weight/day
- Group 3: 0.60 mg of diflubenzuron/kg of body weight/day
- Group 4: control (untreated: fed in the same manner minus the active ingredient)

All animals received the same dose of product based on their weight, beginning on study day 0 through study day 9. All animals consumed fully the treatment in their first half of their diet (morning feeding). The remainder of the diet was administered in the afternoon. Clean water was provided *ad libitum*. Manure samples (~200 g) from each animal was collected in bags, beginning in day 0 (pretreatment) through day 9. For each goat on each collection day, three house fly (*Musca domestica*) bioassay cups were prepared using the feces on a given collection day. Manure samples were frozen to kill any arthropod fauna that may have been present in the feces prior collection and then thawed prior to use. Water was added to feces at rate of approximately 100 ml/50 g of feces and was mixed thoroughly by hand to ensure a homogeneous sample mixture. Approximately 50 g of amended manure mixture was placed in each plastic bioassay cup. House fly larvae (less than 24 hours old) were collected, and 50 larvae were placed in each cup containing a feces sample. Bioassay cups were then placed into a #4 paper bag, with the top folded in triplicate and stapled to prevent adult house fly escape. The paper bags were held at 80 °F, 12:12 LD, and approximately 40% RH, for a period of 3 weeks. Each bioassay cup was moistened with approximately 5 ml of water every 72 hours, until pupae were observed, to minimize desiccation of larvae.

Fly emergence was determined by counting the number of dead adult flies in each bioassay container, approximately 3 weeks after infestation. The percent efficacy of the three treatment groups was calculated with the following equation:

$$\% \text{ Efficacy} = \left(\frac{\text{Control AAFE} - \text{Treatment AAFE}}{\text{Control AAFE}}\right) \text{x} 100$$

"AAFE" stands for "average adult fly emergence," the averages being of individual emergence data for each of the six animals (18 cups) within the specific group per day in question.

(3) **Results:** State the results for control and treatment groups.

Group 1 (0.40 mg diflubenzuron/kg of body weight/day)
Average percent adult fly emergence was 30.78%, 35.46%, 4.66%, 4.34%, 2.44%, 3.34%, 6.44%, 1.44%, 3.34%, and 1% on days 0, 1, 2, 3, 4, 5, 6, 7, 8, and 9, respectively. Percent efficacy was -4.01%, 92.42%, 89.20%, 94.82%, 95.11%, 92.77%, 97.79%, 88.42% and 98.36% on days 1, 2, 3, 4, 5, 6, 7, 8, 9, respectively.

Group 2 (0.50 mg diflubenzuron/kg of body weight/day)
Average percent adult fly emergence was 46.78%, 38.66%, 7.78%,1.78%, 0.66%, 1.44%, 4%, 4.22%, 7.88% and 6.22% on days 0, 1, 2, 3, 4, 5, 6, 7, 8, and 9, respectively. Percent efficacy was 46.78%, -16.39%, 87.36%, 95.57%, 98.59%, 97.88%, 95.51%, 93.54%, 72.59% and 89.80% on days 1, 2, 3, 4, 5, 6, 7, 8 and 9, respectively.

Group 3 (0.60 mg diflubenzuron/ kg of body weight/day)
Average percent fly emergence was 49%, 25.56%, 7.12%, 2.66%, 0.44%, 3.66%, 0.88%, 0.88%, 2% and 0.44% on days 0, 1, 2, 3, 4, 5, 6, 7, 8 and 9, respectively. Percent efficacy was 23.08%, 88.45%, 93.35%, 99.06%, 94.63%, 99.00%, 98.64%. 93.05% and 99.27% on days 1, 2, 3, 4, 5, 6, 7, 8 and 9, respectively.

Group 4 (untreated control)
Control fly emergency was on average 39.34%, 42.88%, 59.22%, 60.34%, 55.66%, 59.12%, 59.88%, 62.12%, 66.12% and 57.78% on days 0, 1, 2, 3, 4, 5, 6, 7, 8, and 9, respectively.

Overall, a > 90% reduction in adult house fly emergence numbers was observed by day 2 of the treatment compared to controls. Average control fly emergence exceeded >50% of the original inoculum and data showed that emergence in the treatments was at least an order of magnitude lower than controls.

(4) **Conclusion:** This MRID is **acceptable**; the data submitted supports efficacy of daily doses of the labeled rate (0.4 mg diflubenzuron/kg of body weight) to control house flies on goat and sheep, but not deer, manure. The data indicated that daily doses of RF2279 015 DFB BAL at 0.40 mg of diflubenzuron/kg of body weight/day to goats reduced numbers of adult house flies that emerged from manure during treatment by ≥90% compared to controls; therefore these data can be bridged to support the label rate for RMI-2011-D 0.04% Diflubenzuron Cattle Supplement. Data can be bridged between Bovid species (goat and sheep) because they occupy similar habitats and graze on similar foods. Data cannot be bridged from goats to deer (Cervids) because they live in different habitats

and require higher quality and less abrasive food than Bovids due to differences in their teeth (Heywood, 2009). Feeding habits difference (different food) between Cervids and bovids may affect feces fermentation needed for house fly development.

IV. EXECUTIVE DATA SUMMARY:

(A)The data submitted supports efficacy of daily doses of the labeled rate (0.4 mg diflubenzuron/kg of body weight) to control stable and house flies on goat and sheep, but not deer, manure. Data can be bridged between Bovid species (goat and sheep) because they occupy similar habitats and graze on similar foods. Data cannot be bridged from goats to deer (Cervids) because they live in different habitats and require higher quality and less abrasive food than Bovids due to differences in their teeth (Heywood, 2009). Feeding habits difference (different food) between Cervids and bovids may affect feces fermentation needed for stable and house fly development. Thus, deer claims are not supported. General fly claims (e.g. "manure breeding fly/flies") are not supported by the data.

V. LABEL RECOMMENDATIONS:

(1) **List changes to the directions for use**:

- All DFU and claims must be specified so that is clear that the product is efficacious against horn flies, face flies, house flies and stable flies for cattle, horses and swine; and stable flies and house flies for sheep and goats or refer to as "listed" once the species have been specified.
- General fly claims (e.g. "manure breeding flies") are not supported.
- Data do not support claims in deer.

(2) **The following marketing claims are acceptable:**
A nutritional supplement containing Diflubenzuron Insect Growth Regulator for continuous feeding to (cattle) (horses) (equine) (swine) (sheep) (and/or) (goats) through the fly season.

A [nutritional] premix containing [Diflubenzuron Insect Growth Regulator] for inclusion in [(beef) (and) (dairy) (cow) (heifer) (horse) (swine) (nursery) (grow-finish) (breeding stock) (Total mixed rations)(TMR's)(rations)] [to] [that] prevent(s) the emergence of (horn flies) (face flies) (house flies) (stable flies) from (manure)(waste) of treated (cattle) (horses)(equine) (and) (swine)

A [nutritional] premix containing [Diflubenzuron Insect Growth Regulator] for inclusion in (sheep) (goat) (Total mixed rations)(TMR's)(rations)] [to] [that] prevent(s) the emergence of (house flies) and (stable flies) from (manure)(waste) of treated (sheep)(and)(goats)

(Can be used as) part of [(an integrated)(a total)(a complete)] (fly control)(pest management) program

(3) **The following marketing claims are unacceptable:**

- All marketing claims for deer
- General fly claims (e.g. "manure breeding" flies)
- Claims against horn and face flies for sheep and goats

(4) The following MRIDs should be removed from the data matrix, as they are classified as "unacceptable" to support the product: N/A